

MALARIA PRIZE WINNERS

RONALD ROSS

In 1902, Dr Ronald Ross was awarded the Nobel Prize in Physiology or Medicine "for his work on malaria, by which he has shown how it enters the organism and thereby has laid the foundation for successful research on this disease and methods of combating it."(1)

The son of a British general in the Indian Army, Dr Ross was born in 1857 and spent his early years in India.(1) He was educated in England, where he developed an interest in poetry, literature, music, and mathematics.(2) Despite his desire to become a writer, Dr Ross acquiesced to pressure from his father to pursue a career in medicine and serve in the Indian Medical Service.(2) After completing his medical studies in London, Dr Ross accepted a post as the surgeon on a transatlantic ship.(2) During this period, he studied for and passed the qualifying examinations that enabled him to enter the Indian Medical Service in 1881.(1,2) Early in his career, he held appointments in Madras, Burma, and the Andaman Islands, where much of his work involved treating soldiers with malaria, many of whom died because they failed to get treatment.(3)

During his early days in Bangalore, Dr Ross was bothered by mosquitoes invading his bungalow and noticed that they swarmed around a barrel of standing water just outside his window; the water was teeming with mosquito larvae.(3) Dr Ross noted that emptying the barrel of water reduced the number of mosquitoes.(3) Unfortunately, when he communicated this discovery and his views on ways to control the mosquito population, he was met with indifference from his superiors.(3)

For centuries, malaria was believed to be spread by the stench from decaying organic matter called miasma.(4,5) Dr Louis Pasteur and Dr Robert Koch thought that malaria was caused by bacteria, but results from their research were not reproducible.(5) In 1880, Dr Alphonse Laveran observed a parasite in the blood from a patient infected with malaria and challenged the bacterial theory, proposing instead a parasite theory.(4,5) How the disease was transmitted was still unknown. In 1876, Sir Patrick Manson had discovered "that the parasite of filariasis, the disease that causes elephantiasis, was taken from human blood by female mosquitoes and continued its growth within the mosquito's abdomen."(5) After observing malaria parasites under a microscope, he believed Dr Laveran's theory that malaria was a parasitic disease and suggested that mosquitoes acquired the malaria parasites from infected human blood and incubated them: the mosquito-nurse

hypothesis.(5)

Dr Ross, meanwhile, had written several articles supporting the bacterial theory of malaria. In 1894, while on home leave, Dr Ross visited Dr Manson in London.(5) After Dr Manson showed him the Plasmodium parasite in the blood of a human being infected with malaria, Dr Ross was convinced that Manson's mosquito-nurse theory was valid.(5) Realizing that Dr Ross would be returning to duty in India, where malaria was common, Manson urged him to pursue research to support the mosquito-nurse theory.(5)

When Dr Ross, newly married, returned to India, he became a staff surgeon in Bangalore. There, he sought to prove the hypotheses advanced by Dr Laveran and Dr Manson that mosquitoes were involved in the spread of malaria.(2) Dr Ross made his landmark discovery on 20 August 1897.(1) When he dissected an Anopheles mosquito that had previously fed on a patient infected with malaria, he found malaria parasites that were growing in the mosquito.(2-4) After being transferred to Calcutta, Dr Ross continued his research and demonstrated that mosquitoes could serve as intermediate hosts for bird malaria.(2,4) He found that malaria parasites could develop in mosquitoes that had fed on infected birds.(2,4) Then the malaria parasites migrated to the salivary glands of the mosquitoes, allowing them to infect other birds during subsequent feedings.(2,4)

On 06 July 1898, Dr Ross summarized his 3 years of careful research, stating that "Malaria is conveyed from a diseased person or bird to a healthy one by the proper species of mosquito, and is inoculated by its bite."(5) His research demonstrated the lifecycle of malaria parasites in mosquitoes.(1)

Resigning from the Indian Medical Service in 1899,



Ronald Ross

The Nobel Prize in Physiology or Medicine 1902

Biography



Ronald Ross was born on May 13, 1857, as the son of Sir C.C.G. Ross, a General in the English army. He commenced the study of medicine at St. Bartholomew's Hospital in London in 1875; entered the Indian Medical Service in 1881. He commenced the study of malaria in 1892. In 1894 he determined to make an experimental investigation in India of the hypothesis of Laveran and Manson that mosquitoes are connected with the propagation of the disease. After two and a half years' failure, Ross succeeded in demonstrating the life-cycle of the parasites of malaria in mosquitoes, thus establishing the hypothesis of Laveran and Manson. In 1899 he joined the Liverpool School of Tropical Medicine under the direction of Sir Alfred Jones. He was immediately sent to West Africa to continue his investigations, and there he found the

Nobel Foundation biography of Ronald Ross

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Dr Ross returned to England and to work for the newly established Liverpool School of Tropical Medicine.(1) In this role, he began investigating and devising anti-malaria schemes in West Africa, including developing measures to control malaria, and this research took him to Ismailia, Egypt, Panama, Greece, and Mauritius.(1,2)

Dr Ross wrote extensively about malaria, including in 1911 a book titled *The Prevention of Malaria*.(1) Ross was also "a mathematician, epidemiologist, sanitarian, editor, novelist, dramatist, poet, amateur musician, composer, and artist."(2)

In recognition of Ross' Nobel Prize winning work that laid the foundation for research into methods for combating the disease, the Prince of Wales funded the Ross Institute and Hospital for Tropical Diseases in London. The focus of the institute was the nature, transmission, treatment, and prevention of tropical diseases. Dr Ross was the director in chief from 1926 until his death in 1932.

References

- 1.Nobel Foundation. The Nobel Prize in Physiology or Medicine 1902. At nobelprize.org. Accessed 07 Dec 2006.
- 2.Centers for Disease Control and Prevention. Ross and the Discovery that Mosquitoes Transmit Malaria Parasites. At www.cdc.gov/malaria/history/ross.htm Accessed 11 Dec 2006.
- 3.Malaria Site. Sir Ronald Ross (1857 - 1932). At www.malariasite.com/malaria/ross.htm. Accessed 11 Dec 2006.
- 4.A Brief History of Malaria. In: Arrow KJ, Panosian C, Gelband H, eds. *Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance*. National Academies Press; 2004.
- 5.Guillemain J. Choosing scientific patrimony: Sir Ronald Ross, Alphonse Laveran, and the mosquito-vector hypothesis for malaria. *J Hist Med.* 2002;57: 385-409.

By DG Betterton-Lewis

ALPHONSE LAVERAN

Charles Louis Alphonse Laveran secured his place in history when he identified the organism that caused malaria. A military physician and expert in parasitic diseases endemic to tropical climates, Dr Laveran received the 1907 Nobel Prize in Medicine or Physiology "in recognition of his work on the role played by protozoa in causing diseases."(1)

On 18 June 1845, Dr Laveran was born in Paris to Louis Theodore Laveran and Guenard de la Tour Laveran.(2) He grew up in a family that was steeped in the traditions of medicine and military service; Dr Laveran's father was a military physician who later held an academic post, his paternal grandfather was a physician, and both his maternal grandfather and great grandfather were senior army commanders. Dr Laveran grew up in Paris and Algeria, attending the College Saint Baube and the Lycee Louis-le-Grand.

Dr Laveran enrolled at the Public Health School at Strasbourg in 1863, graduating in 1866. In 1874, after medical service in Strasbourg and after the Franco-German War, when he was taken prisoner, Dr Laveran won an examination-based appointment to the position once held by his father: the Chair of Military Diseases and Epidemics at the Ecole de Val-de-Grace.

Transferred to a military hospital in Constantine, Algeria in 1878, Dr Laveran saw entire platoons decimated by malaria. With an ample supply of fresh corpses available for autopsy, Dr Laveran searched blood, brains, and spleens for clues to the origin of the disease. The tissues and blood were loaded with the characteristic black pigments first described by Lancisi and Meckel in 1847, but nothing in the samples suggested to him a cause for malaria.

Dr Laveran redirected his efforts to live subjects. In blood samples taken from infected soldiers, he routinely saw only the black, pigmented blood cells associated with malaria. But on 06 November 1880, Dr Laveran saw in the blood of one sick patient a series of pigmented and non-pigmented bodies.(3) The largest, a crescent-shaped organism, used its flagella to thrash around in the blood. Dr Laveran recognized that the previously unknown bodies represented different stages in the lifecycle of the same organism, the organism that caused malaria. Convinced that it was a protozoan and not a bacterium, Dr Laveran named the new parasite *Oscillaria malariae*. This name was dropped 4 years later when Marchiafava and Celli misclassified the parasite as a member of the *Plasmodium* species.

By year's end Dr Laveran had communicated his results to researchers in Algeria, France, and Italy.

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A friend in Algeria, Dr E Richard, confirmed Dr Laveran's findings, and took them a step further. In the red blood cells of infected patients, Dr Richard found an earlier stage of the parasite and concluded that the organism developed inside red blood cells until it was mature enough to lyse the cells and to survive.

Not everyone believed that Dr Laveran's protozoa caused malaria. Pasteur's germ theory for disease (that is, bacteria cause diseases) dominated the thinking in the 1880s. It was especially hard to consider a non-bacterial source, since in 1879 Klebs and Tomassi-Crudeli had reported that the culprit was the bacterium *Bacillus malariae*.(3)

According to Dr Laveran: "The heaeatozoon which I gave as the agent of malaria did not resemble bacteria, and was present in strange forms, and in short it was completely outside the circle of the known pathogenic microbes, and many observers not knowing how to classify it found it simpler to doubt its existence."(4)

To convert the non-believers, Dr Laveran traveled to Italy in 1882, where he confirmed the existence of the parasite in the blood of infected soldiers from the Roman Campagna. Following his return to Paris and the Ecole Val-de-Grace in 1884, Dr Laveran invited Pasteur and Emile Roux to examine the blood of a French soldier infected with a rare case of malignant malaria. Reportedly, Pasteur was converted on the spot, and 5 years later Dr Laveran's work received official acceptance, when he was awarded the Breat Prize from the French Academy of Sciences.(5)

After retiring from the Army in 1896, Dr Laveran joined the Pasteur Institute in Paris as the Honorary Chief of Research. He continued working on tropical diseases, especially those caused by parasites such as trypanosomes and leishmania. With money received from his Nobel Prize, Dr Laveran established the Laboratory of Tropical Medicine at the Institute, remaining there until he died on May 18, 1922. A prolific author, in his lifetime Dr Laveran published nearly 600 scientific papers and wrote 6 books.

References

- 1.The Nobel Prize In Physiology or Medicine. Nobel Foundation Web site. At: nobelprize.org/nobel_prizes/medicine/laureates/1907/index.html. Accessed 03 Dec 2006.
- 2.Biography of Alphonse Dr Laveran. Nobel Foundation Web site. At http://nobelprize.org/nobel_prizes/medicine/laureates/1907/Dr Laveran-bio.html. Accessed 03 Dec 2006.
- 3.Charles Louis Alphonse Dr Laveran. Malaria Site. At www.malariasite.com/malaria/Dr Laveran.htm. Accessed 03 Dec 2006.

4.Protozoa as Causes of Diseases. Nobel Foundation Web site. At nobelprize.org/nobel_prizes/medicine/laureates/1907/Dr Laveran-lecture.html. Accessed 03 Dec 2006.

5.Dr Laveran and the Discovery of the Malaria Parasite. Department of Health and Human Services. Centers for Disease Control and Prevention Web site. At www.cdc.gov/malaria/history/Dr Laveran.htm. Accessed 14 Dec 2006.

By *TM Zydowsky*



Biography



Charles Louis Alphonse Laveran was born in Paris on Jun 18, 1845 in the house which was formerly No. 19 rue de l'Est but later became, when this district was rebuilt, an hotel at N 125, Boulevard St. Michel.

Both his father and paternal grandfather were medical men. father, Dr. Louis Théodore Laveran, was an army doctor and Professor at the École de Val-de-Grâce, his mother, *née* Guénard de la Tour, was the daughter and granddaughter of high-ranking army commanders. When he was very young, Alphonse went with his family to Algeria. His father returned France as Professor at the École de Val-de-Grâce, of which h became Director with the rank of Army Medical Inspector.

Alphonse, after completing his education in Paris at the Collège Saint-Barthélemy and later at

Nobel Prize website, nobelprize.org.

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Year Nobel Prize in Physics Nobel Prize in Chemistry Nobel Prize in Physiology or Medicine Nobel Prize in Literature Nobel Prize in Peace



Nobel Lecture

Nobel Lecture, December 11, 1907

Protozoa as Causes of Diseases

My scientific colleagues of the Caroline Institute having done me the very great honor of awarding me the Nobel Prize in Medicine this year for my work on diseases due to Protozoa, the regulations of the Nobel Foundation oblige me to give a summary of my researches on this question.

I must however go back a little in order to explain how I was led to concern myself with pathogenic protozoa.

In 1878 after having finished my course of instruction at the School of Military Medicine Val-de-Grâce, I was sent to Algeria and put in charge of a department of the 1st Bône. A large number of my patients had malarial fevers and I was naturally led to study these fevers of which I had only seen rare and benign forms in France.